

Goldstein et al.
Application No.: 10/045,903
Page 2

PATENT

Amendments To The Specification

Please replace the clause beginning at page 5, line 3 with the following amended clause:

--(x) cycloalkylalkyl, ~~cycloalkylalkynyl~~ cycloalkylalkenyl and
cycloalkylalkynyl, all optionally substituted with alkyl, halo,
hydroxy or amino; --

Please replace the clause beginning at page 22, line 24 with the following amended
clause:

-- (l) cycloalkylalkyl, ~~cycloalkylalkynyl~~ cycloalkylalkenyl and
cycloalkylalkynyl, all optionally substituted with alkyl, halo, hydroxy or
amino; --

Please replace the paragraph beginning at page 27, line 12 with the following amended
paragraph:

--Reaction of the 2-keto-3-phenylaminoacrylonitrile of formula 2 with a hydrazine of
formula 3 provides a 5-amino-4-ketopyrazole of formula 4. This reaction is generally carried out in
a polar solvent such as ethanol, isopropanol, and the like. Aryl/heteroaryl hydrazines of formula
[[2]] 3 such as 2- or 3-chlorophenylhydrazine, 2-, 3-, or 4-fluorophenylhydrazine, phenylhydrazine,
2-hydrazinopyridine, 2-hydrazinobenzothiazole, 2-hydrazinoquinoline etc., are commercially
available. --

Please replace the paragraph beginning at page 30, line 6 with the following amended
paragraph:

--A compound of Formula (I) where R³ is heteroalkenyl, heteroalkynyl, heterocyclalkenyl
or heterocyclalkynyl can be prepared by reacting a compound of formula 4 where Z is halo with a
heteroalkene, heteroalkyne, heterocyclalkene or heterocyclalkyne respectively in the presence of

HALLR6 #125320 v1

Goldstein et al.
Application No.: 10/045,903
Page 3

PATENT

a palladium (II) catalyst such as dichlorobis(triphenylphosphine)-palladium (II) in an organic base such as diisopropylamine, and the like. Heteroalkenes, heteroalkynes such as allyl alcohol, propargyl alcohol, 3-butyne-1-ol, propargylamine are commercially available. Heterocyclylalkyne can be prepared by reacting an alkynyl halide with a heterocycle. For example, 2-morpholin-1-ylprop-1-yne 3-morpholin-1-ylprop-1-yne can be prepared by reacting propargyl bromide with morpholine. Reduction of the double or triple bond under catalytic hydrogenation reaction conditions provides the corresponding compound of Formula (I) where R³ is a heterocyclylalkyl or heteroalkyl group. --

Please replace the paragraph beginning at page 64, line 14 with the following amended paragraph:

--Replacing piperidine in Step[[1]] 2 above with:

morpholine,

N-methylpiperazine,

4-hydroxypiperidine,

2-aminopyridine,

3-aminopyridine,

4-methylimidazole,

3-aminopyrazole, and

2-methylimidazole;

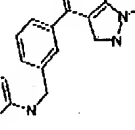
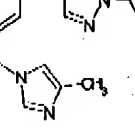
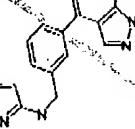
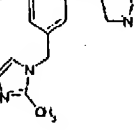
the following compounds were obtained

HALLR6 #125320 v1

Goldstein et al.
Application No.: 10/045,903
Page 4

PATENT

Structure	CPD #	HRMS MW	MP1
	131	398.411	127.3-128.5
	132	484.376	238.2-238.6
	133	412.430	141.5-145.5
	134	405.406	

Structure	CPD #	HRMS MW
	135	405.406
	136	393.395
	137	508.405
	138	507.417

Please replace the paragraph beginning at page 77, line 8 with the following amended paragraph:

--The ability of the compounds of this invention to inhibit the TNF- α release was determined using a minor modification of the methods ~~described in~~ described in Blifeld, C. et al. *Transplantation*, Vol. 51(2), 498-503, (1991). --

HALLR6 #125320 v1